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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,581	06/05/2001	Gary M. Fader	BB-1339	6372

7590 03/10/2004

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EXAMINER	
RAMIREZ, DELIA M	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/857,581	FADER ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,11-19,26,29-33 and 51-69* is/are pending in the application.

4a) Of the above claim(s) *51-69* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,11-19,26,29-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Claims 1, 3-4, 11-19, 26, 29-33, 51-69 are pending.

Applicant's amendment of claims 1, 3-4, 11-14, 26, 29-31, cancellation of claims 5-10, 28, 44-45, and addition of claims 51-69 in a communication filed on 12/5/2003 are acknowledged.

Applicant's submission of a declaration by Dr. Brian McGonigle under 37 CFR 1.131 in a communication filed on 12/5/2003 is acknowledged.

As asserted by Applicants on page 44, paragraph 4 of the Remarks section in a communication filed on 12/5/2003, new claims 51-69 are directed to nucleic acids encoding the polypeptides of SEQ ID NO: 2, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 61, 55, 57, 59, and 48, respectively. These claims are now drawn to non-elected polynucleotides in Groups a, c-t. It was indicated in previous Office Action Paper No. 7, mailed on 6/3/2003, that the polynucleotides of Groups a, c-t do not share a common property or activity. In regard to Groups c-f, n-t (polynucleotides encoding the polypeptides of SEQ ID NO: 16, 18, 20, 22, 38, 40, 48, 55, 57, 59 and 61), it is noted that by visual inspection it was found that at least the polypeptides of SEQ ID NO: 16, 18, 20, 22, 40, 48, 55, 57, 59, and 61 differ from the consensus sequence of SEQ ID NO: 66 in at least 2 residues since they have a Phe, Ser or Leu residue at position 1 and either a Thr, Ala or a Ser residue at position 9 whereas the consensus sequence of SEQ ID NO: 66 has a Met residue at position 1 and a Leu residue at position 9. Therefore, the polynucleotides in Groups c-f, n-t are not even structurally related by the polypeptides they encode to polynucleotides encoding polypeptides having the consensus sequence of SEQ ID NO: 66. Assuming that the polynucleotides encoding the polypeptides of SEQ ID NO: 2, 24, 26, 28, 30, 32, 34, 36 (Groups a, g-m) encode polypeptides having the consensus sequence of SEQ ID NO: 66, as indicated in previous Office Action Paper No. 7, there is lack of unity regarding these Groups since a consensus polynucleotide which encompass all the polynucleotides of Groups a, g-m will have substantially less common structural

elements due to the degeneracy of the genetic code. Furthermore, each of these polynucleotides may be detected by different nucleic acid probes. As such, a nucleic acid probe which would detect one polynucleotide may not detect another, even if they encode proteins of similar function. Newly added claims 51-69 are withdrawn from consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Specification

1. The specification remains objected to since the sequence listing in page 50 indicates residues at positions 293 and 294 of SEQ ID NO: 66 as "unsure", however in page 53, positions 292 and 293 are marked as "Xaa" whereas position 294 is an Ile residue.

2. The specification remains objected to because of the recitation in page 42 of "Xaa_{293} is Glu or Asp". It is noted that according to Appendix A, provided by Applicants in Paper No. 6, position 293 is more likely to be a Gln or a His residue instead of a Glu or Asp residue as recited in the specification.

3. It is noted that while Applicants assert in the Remarks section of the response filed on 12/5/2003 that the specification and the sequence listing have been amended in response to previous Office Action Paper No. 7, according to the record, no new sequence listing has been filed and no amendments to page 42 have been filed. Amendments to the specification only address the issue of hyperlinks in the specification.

Drawings

4. The formal drawings submitted 12/5/2003 are accepted by the Examiner.

Claim Objections

5. Claim 4 is objected to due to the recitation of "wherein the nucleic acid is not the nucleic acid sequence set forth in SEQ ID NO: 9". For clarity, it is suggested that the term be amended to recite "wherein the nucleic acid does not have the nucleic acid sequence set forth in SEQ ID NO: 9". Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 14, 11-19, 26, 29-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 1 (claims 11-19, 26, 29-33 dependent thereon) is indefinite in the recitation of "wherein the nucleic acid fragment does not have the ....." as there is no antecedent basis for the term "nucleic acid fragment". For examination purposes, it will be assumed that the term reads "wherein the nucleic acid does not have....". Correction is required.

9. Claim 1 (claims 11-19, 26, 29-33 dependent thereon) are indefinite in the recitation of Xaa_{294} is Thr or Ile" since according to the sequence listing, the amino acid residue corresponding to position 294 is Ile, i.e. position 294 is defined in the sequence listing. For examination purposes, no patentable weight will be given to the term. Correction is required.

10. Claim 14 is indefinite in the recitation of "wherein the second chimeric polynucleotide comprises a chimera containing a polynucleotide encoding the maize R region, wherein the R region is between polynucleotide encoding the maize C1 DNA binding domain and the maize C1 activation domain" for the following reasons. While Applicants remarks have been considered regarding the different genes

encoding the R region and the C1 domains, as written, it is unclear as to how the term "wherein the R region...." further limits the claim since one cannot determine if the polynucleotide encoding the maize C1 DNA binding domain and the maize C1 activation domain are part of the chimera. It is noted that there is no recitation in the claim that relates the nucleic acid encoding a polypeptide that regulates expression of at least one enzyme of the phenylpropanoid pathway (recited in claim 13), and the polynucleotide encoding the maize C1 DNA binding domain and the maize C1 activation domain. From page 6 of the specification, lines 7-14, it appears that the second chimera can be a nucleic acid which encodes a transcription factor. Thus, it is assumed that the claims refer to a host cell transformed with a chimeric polynucleotide encoding the maize transcription factor protein R, the maize transcription factor C1 DNA binding domain, and the maize transcription factor C1 activation domain, wherein the polynucleotide encoding the maize transcription factor protein R is between the polynucleotides encoding the maize transcription factor C1 DNA binding domain and the maize transcription factor C1 activation domain. The Examiner has interpreted maize R region as equivalent to maize transcription factor R (also known in the art as cofactor R, or basic helix-loop-helix bHLH protein R), however Applicants are requested to clarify the term since it can also be interpreted as a fragment of the maize transcription factor R. If the Examiner's assumptions are correct, it is suggested that the claim be amended to recite "the transformed host cell of claim 13 wherein said chimeric polynucleotide encodes the maize transcription factor protein R, the maize transcription factor C1 DNA binding domain, and the maize transcription factor C1 activation domain, and wherein the polynucleotide encoding the maize transcription factor protein R is between the polynucleotides encoding the maize transcription factor C1 DNA binding domain and the maize transcription factor C1 activation domain" or similar. Correction/clarification is required.

Claim Rejections - 35 USC § 112, First Paragraph

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1, 11-19, 26, 29-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 1 and 11, as amended, are now directed to a genus of nucleic acids encoding a polypeptide having isoflavone synthase activity having the amino acid sequence of SEQ ID NO: 66, wherein the nucleic acid does not have the nucleotide sequence set forth in SEQ ID NO: 9, and wherein 67 positions within the sequence of SEQ ID NO: 66 are defined. Claims 12-19, 26, 29-33 are directed to host cells comprising the genus of polynucleotides of claim 11, or methods to altering the expression of isoflavone synthase in a host cell with the polynucleotides of claim 11. While the Examiner has found support for a genus of nucleic acids encoding isoflavone synthases wherein said nucleic acids do not have the nucleotide sequence set forth in SEQ ID NO: 9, the Examiner is unable to locate adequate support in the specification for a genus of nucleic acids encoding a polypeptide having isoflavone synthase activity having the amino acid sequence of SEQ ID NO: 66, wherein the nucleic acid does not have the nucleotide sequence set forth in SEQ ID NO: 9, and wherein 67 positions within the sequence of SEQ ID NO: 66 are defined. Thus there is no indication that the genus of nucleic acids encompassed by amended claim 1, as described above, were within the scope of the invention as conceived by Applicants at the time the application was filed. Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

13. Claims 3-4 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

14. This rejection has been discussed at length in Paper No. 7, mailed on 6/3/2003.

15. Applicants argue that the specification discloses the amino acid sequences of 20 plant isoflavone synthases and that the consensus sequence in the specification shows that there are 460 non-variant amino acids and 61 amino acids which vary among the 20 amino acid sequences, therefore only 8.5% of the 521 amino acids in a plant isoflavone synthase vary.

16. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the instant rejection. While the Examiner acknowledges the consensus sequence of SEQ ID NO: 66 and the disclosure of the amino acid sequences of 20 plant isoflavone synthases, the Examiner disagrees with Applicant's contention that the information provided is sufficient to adequately describe the claimed genus of polynucleotides. Claims 3-4, as amended, are directed to (1) a genus of polynucleotides encoding any (from any source) isoflavone synthase capable of converting 2S-flavone into an isoflavonoid, or (2) a genus of polynucleotides encoding any (from any source) isoflavone synthase capable of converting 2S-flavone into an isoflavonoid, wherein the nucleic acid does not have the nucleotide sequence of SEQ ID NO: 9. Thus, the claims are not limited to polynucleotides encoding the isoflavone synthases having the features defined in the specification. While one could argue that the disclosure of the amino acid sequences of 20 plant isoflavone synthases and a consensus sequence for these 20 amino acid sequences is sufficient to adequately describe the genus of polynucleotides claimed, it is noted that there is no information in the specification or the art as to whether this consensus sequence is applicable to any isoflavone synthase from any source or if all isoflavone synthases will have 521

amino acids. It is also noted that several of the isoflavone synthases disclosed do not have 521 amino acids. As indicated previously in Paper No. 7 and reiterated herein, the genus of nucleic acids claimed is a large variable genus with the potentiality of comprising many structurally distinct nucleic acids as it encompasses not only the nucleic acids encoding any plant isoflavone synthase but any nucleic acid encoding any isoflavone synthase.

While a sufficient written description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by their amino acid sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus., in the instant case, there is no structural feature which is representative of all the members of the genus of nucleic acids recited in the claim 3. In regard to claim 4, the only structural limitation recited does not constitute a substantial portion of the genus as the remaining nucleic acids which do not have the sequence of SEQ ID NO: 9 are completely undefined and the specification does not define the structural features for the remaining members of the genus to be selected.

The art as evidenced by the teachings of Bork, Witkowski et al. , Van de Loo et al., Broun et al. and Seffernick et al., as discussed previously, clearly teach the unpredictability of the art as it relates to accurate determination of function based solely on structural homology. In the instant case, one cannot reasonably conclude that any isoflavone synthase from any organism will have an amino acid structure which is approximately 90% identical to that of the consensus isoflavone synthase of SEQ ID NO: 66. For inventions in an unpredictable art, which is the case herein, adequate written description of a genus which embraces species with the potentiality of being structurally variable, cannot be achieved by disclosing a few species within the genus. Therefore, one cannot reasonably conclude that the claimed invention is adequately described.

17. Claims 3-4 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids encoding isoflavone synthases, wherein said isoflavone synthases have the sequence of SEQ ID NO: 66 and the specific amino acids recited in claim 1, does not reasonably provide enablement for any nucleic acid (1) encoding any isoflavone synthase capable of converting 2S-flavone into an isoflavonoid, or (2) encoding any isoflavone synthase capable of converting 2S-flavone into an isoflavonoid, wherein said nucleic acid does not have the sequence set forth in SEQ ID NO: 9. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

18. This rejection has been discussed at length in Paper No. 7, mailed on 6/3/2003.

19. Applicants argue that the specification discloses the amino acid sequences of 20 plant isoflavone synthases and that the consensus sequence in the specification shows that there are 460 non-variant amino acids and 61 amino acids which vary among the 20 amino acid sequences, therefore only 8.5% of the 521 amino acids in a plant isoflavone synthase vary.

20. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. As indicated above, the claims as amended are directed to a nucleic acid (1) encoding any isoflavone synthase capable of converting 2S-flavone into an isoflavonoid, or (2) encoding any isoflavone synthase capable of converting 2S-flavone into an isoflavonoid, wherein said nucleic acid does not have the sequence set forth in SEQ ID NO: 9. The scope of the claims is not commensurate with the enablement provided in view of the extremely large number of polynucleotides of unknown structure encompassed by the claims. The teachings of the specification, while providing the structures of 20 plant isoflavone synthases and a consensus structure for these plant isoflavone synthases, are not deemed sufficient to enable the full scope of the claims since, in the absence of any information as to (1) whether all isoflavone synthases have the consensus sequence of SEQ ID NO: 66, (2) whether all isoflavone synthases will have a structure at least 90% identical to the consensus isoflavone synthase of SEQ ID

NO: 66, or (3) which are the critical structural elements which must be present in all polynucleotides encoding isoflavone synthases, and in view of the unpredictability of the art regarding accurate determination of function based on structural homology, one of skill in the art would have to go through the burden of undue experimentation to isolate/make those polynucleotides encoding those isoflavone synthases which do not share the consensus sequence of SEQ ID NO: 66, as encompassed by the claims. Therefore, one cannot reasonably conclude that the full scope of the claimed invention is enabled by the disclosure.

Claim Rejections - 35 USC § 102

21. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

22. Claims 1, 3-4, 11-12, 15, 26 and 29 remain rejected under 35 U.S.C. 102(a) as being anticipated by Steele et al. (Archives of Biochemistry and Biophysics, July 1, 1999; cited in the IDS). This rejection has been discussed in previous Office Action Paper No. 7.

23. Applicants submit a declaration under 37 CFR 1.131 by Dr. Brian McGonigle in a communication filed on 12/5/2003. In this declaration, Dr. McGonigle affirms that Applicants were the first, to their knowledge, to conceive and reduce to practice a polynucleotide having isoflavone synthase activity and that their work was completed prior to the publication of Steele et al. While the submission of this declaration is acknowledged, it is noted that a properly executed declaration under 37 CFR 1.131 must be signed by all inventors. See MPEP 715.04. Since the declaration is signed only by inventor Brian McGonigle, it is deemed improperly executed and has not been considered. Thus, this rejection is maintained for the reasons of record.

24. Claim 3 remains rejected under 35 U.S.C. 102(b) as being anticipated by Siminszky et al. (EMBL accession number AF022462, 1/8/1998; cited in the IDS). This rejection has been discussed in previous Office Action Paper No. 7.

25. Applicants argue that as stated in the Entrez Report, the polynucleotide of Siminszky et al. encodes a protein identified as a cytochrome P450 monooxygenase and that Applicants are the first to disclose that the encoded polypeptide has isoflavone activity.

26. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. While it is acknowledged that the polynucleotide of Siminszky et al. has been disclosed as encoding a cytochrome P450 monooxygenase, it is noted that structure determines function. As such, the isoflavone synthase function of the polypeptide encoded by the polynucleotide of Siminszky et al. is an intrinsic property of said polypeptide. Furthermore, it is noted that at the time of filing, it was known in the art that a cytochrome P-450 monooxygenase could have isoflavone synthase activity. Hashim et al. (FEBS Lett 271(1-2):219-222, 1990; cited in the IDS) teaches that the conversion of liquiritigenin (flavone) into daidzein (isoflavone) was catalyzed by a cytochrome P-450 monooxygenase in P. lobata. See particularly the abstract. Therefore, in P. lobata, a cytochrome P-450 monooxygenase was determined to have isoflavone synthase activity.

Claim Rejections - 35 USC § 103

27. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

28. Claims 17-19 and 30-33 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Steele et al. in view of Siminszky et al. This rejection has been discussed at length in Paper No. 7.

29. Applicants submit a declaration under 37 CFR 1.131 by Dr. Brian McGonigle in a communication filed on 12/5/2003. In this declaration, Dr. McGonigle affirms that Applicants were the

first, to their knowledge, to conceive and reduce to practice a polynucleotide having isoflavone synthase activity and that their work was completed prior to the publication of Steele et al. While the submission of this declaration is acknowledged, the declaration is deemed improperly executed for the reasons set forth above and has not been considered. Thus, this rejection is maintained for the reasons of record.

Conclusion

30. No claim is in condition for allowance.

31. Applicant's amendment of claims 1, 3-4, 11-14, 26, and 29-31 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

32. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 872-9306. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

33. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
March 3, 2004

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600